A dosage-dependent requirement for Sox9 in pancreatic endocrine cell formation.

Journal: Dev Biol

Publication Year: 2008

Authors: Philip A Seymour, Kristine K Freude, Claire L Dubois, Hung-Ping Shih, Nisha A Patel, Maike Sander

PubMed link: 18723011

Funding Grants: Stem Cell Research Training Grant

Public Summary:

Scientific Abstract:
We have previously shown the transcription factor SOX9 to be required for the maintenance of multipotential pancreatic progenitor cells in the early embryonic pancreas. However, the association of pancreatic endocrine defects with the Sox9-haploinsufficiency syndrome campomelic dysplasia (CD) implies additional later roles for Sox9 in endocrine development. Using short-term lineage tracing in mice, we demonstrate here that SOX9 marks a pool of multipotential pancreatic progenitors throughout the window of major cell differentiation. During mid-pancreogenesis, both endocrine and exocrine cells simultaneously arise from the SOX9(+) epithelial cords. Our analysis of mice with 50%-reduced Sox9 gene dosage in pancreatic progenitors reveals endocrine-specific defects phenocopying CD. By birth, these mice display a specific reduction in endocrine cell mass, while their exocrine compartment and total organ size is normal. The decrease in endocrine cells is caused by reduced generation of endocrine progenitors from the SOX9(+) epithelium. Conversely, formation of exocrine progenitors is insensitive to reduced Sox9 gene dosage, thus explaining the normal organ size at birth. Our results show that not only is SOX9 required for the maintenance of early pancreatic progenitors, but also governs their adoption of an endocrine fate. Our findings therefore suggest that defective endocrine specification might underlie the pancreatic phenotype of individuals with CD.